AMENDMENTS TO THE CLAIMS

Claim 1 (Currently amended): A method of modulating the activity of a melanocortin receptor, said method comprising contacting said receptor with a peptide having the formula:

$CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}NAFCYCR_n$ (SEQ ID NO:9)

wherein

X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected amino acids, and

n is zero or one.

Claim 2 (Original): The method of claim 1, wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected from the group consisting of alanine, asparagine, arginine,aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

Claim 3 (Currently amended): The method of claim 1, wherein said peptide is not CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3).

Claim 4 (Currently amended): The method of claim 1, wherein $X^1X^2X^3X^4X^5X^6$ is VRLHES (SEQ ID NO:6) or conservative substitutions thereof.

Claim 5 (Currently amended): The method of claim 4, wherein X1X2X3X4X5X6 is VRLHES (SEQ ID NO:6).

Claim 6 (Currently amended): The method of claim 1, wherein X7X8X9X10X11X12 is LGQQVP (SEQ ID NO:7) or conservative substitutions thereof.

Claim 7 (Currently amended): The method of claim 6, wherein X7X8X9X10X11X12 is LGQQVP (SEQ ID NO:7).

Claim 8 (Currently amended): The method of claim 7, wherein $X^7X^8X^9X^{10}X^{11}X^{12}$ is LGQQVP (SEQ ID NO:7) or conservative substitutions thereof.

Claim 9 (Currently amended): The method of claim 8, wherein $X^7X^8X^9X^{10}X^{11}X^{12}$ is LGQQVP (SEQ ID NO:7).

Claim 10 (Original): The method of claim 1, wherein X^{13} is not a cysteine.

Claim 11 (Original): The method of claim 1, wherein X^{13} is A.

Claim 12 (Currently amended): The method of claim 1, wherein $X^{14}X^{15}X^{16}$ is RFF (SEQ ID NO:8) or conservative substitutions thereof.

Claim 13 (Currently amended): The method of claim 4, wherein $X^{14}X^{15}X^{16}$ is RFF (SEQ ID NO:8) or conservative substitutions thereof.

Claim 14 (Currently amended): The method of claim 8, wherein $X^{14}X^{15}X^{16}$ is RFF (SEQ ID NO:8) or conservative substitutions thereof.

Claim 15 (Original): The method of claim 1, wherein said receptor is in a cell culture.

Claim 16 (Original): The method of claim 1, wherein said receptor is *in vivo* culture.

Claim 17 (Original): The method of claim 1, wherein said receptor is an MC3 receptor.

Claim 18 (Original): The method of claim 1, wherein said receptor is an MC4 receptor.

Claim 19 (Currently amended): A library for screening for modulators of a melanocortin receptor, said library comprising a plurality of polypeptide members wherein said members have the formula:

$$CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}NAFCYCR_n$$ (SEQ ID NO:9)

wherein

X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected amino acids, and

n is zero or one.

Claim 20 (Original): The library of claim 19, wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected from the group consisting of aspartic acid,

alanine, asparagine, arginine,cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

Claim 21 (Currently amended): The method of claim 19, wherein $X^1X^2X^3X^4X^5X^6$ is VRLHES (SEQ ID NO:6) or conservative substitutions thereof.

Claim 22 (Currently amended): The method of claim 21, wherein $X^1X^2X^3X^4X^5X^6$ is VRLHES (SEQ ID NO:6).

Claim 23 (Currently amended): The method of claim 19, wherein $X^7X^8X^9X^{10}X^{11}X^{12}$ is LGQQVP (SEQ ID NO:7) or conservative substitutions thereof.

Claim 24 (Currently amended): The method of claim 23, wherein $X^7X^8X^9X^{10}X^{11}X^{12}$ is LGQQVP (SEQ ID NO:7).

Claim 25 (Currently amended): The method of claim 24, wherein $X^7X^8X^9X^{10}X^{11}X^{12}$ is LGQQVP (SEQ ID NO:7) or conservative substitutions thereof.

Claim 26 (Currently amended): The method of claim 25, wherein $X^7X^8X^9X^{10}X^{11}X^{12}$ is LGQQVP (SEQ ID NO:7).

Claim 27 (Original): The method of claim 19, wherein X^{13} is not a cysteine.

Claim 28 (Original): The method of claim 19, wherein X^{13} is A.

Claim 29 (Currently amended): The method of claim 19, wherein $X^{14}X^{15}X^{16}$ is RFF (SEQ ID NO:8) or conservative substitutions thereof.

Claim 30 (Currently amended): The method of claim 21, wherein $X^{14}X^{15}X^{16}$ is RFF (SEQ ID NO:8) or conservative substitutions thereof.

Claim 31 (Currently amended): The method of claim 25, wherein $X^{14}X^{15}X^{16}$ is RFF (SEQ ID NO:8) or conservative substitutions thereof.

Claim 32 (Currently amended): A method of prescreening for a modulator of a melanocortin receptor, said method comprising:

i) contacting a melanocortin receptor a peptide having the formula:

$CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}NAFCYCR_n$ (SEQ ID NO:9)

wherein

X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected amino acids, and

n is zero or one; and

ii) detecting binding of said peptide to said melanocortin receptor wherein specific binding of said peptide to said melanocortin receptor indicates that said peptide is a potential modulator of said melanocortin receptor.

Claim 33 (Original): The method of claim 32, wherein said peptide is not CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3).

Claim 34 (Original): The method of claim 32, wherein said melanocortin receptor is selected from the group consisting of MC3r, and MC4r.

Claim 35 (Currently amended): A method of screening for a modulator of melanocortin receptor activity, said method comprising:

i) contacting a melanocortin receptor with a peptide having the formula:

$CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}NAFCYCR_n$ (SEQ ID NO:9)

wherein

X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected amino acids, and n is zero or one; and

ii) detecting activity of said melanocortin receptor wherein a difference in activity of said receptor, as compared to a control, indicates that said peptide is a modulator of melanocortin receptor activity.

Claim 36 (Original): The method of claim 35, wherein said control is a negative control comprising the same assay without said peptide.

Claim 37 (Original): The method of claim 35, wherein said peptide is not CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3).

Claim 38 (Original): The method of claim 35, wherein said melanocortin receptor is selected from the group consisting of MC3r, and MC4r.

Claim 39 (Currently amended): A polypeptide comprising a peptide sequence having the formula:

$CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}NAFCYCR_n$ (SEQ ID NO:9)

wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected amino acids, and n is zero or one; and

~~35~~wherein said polypeptide is not AGRP and said polypeptide is not MARP.

Claim 40 (Original): The polypeptide of claim 39, wherein said polypeptide excludes one or more of the final 13 residues of MARP (residues 34-46 of MARP).

Claim 41 (Currently amended): The polypeptide of claim 39, wherein said polyypeptide has the formula:

$CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}NAFCYCR_n$ (SEQ ID NO:9)

wherein

X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected amino acids, and

n is zero or one.

Claim 42 (Original): The polypeptide of claim 41, wherein said polypeptide is not CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3).

Claim 43 (Currently amended): A pharmaceutical composition comprising:

a pharmaceutically acceptable excipient; and

a polypeptide having the formula:

$CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}NAFCYCR_n$ (SEQ ID NO:9)

wherein

X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}, and X^{16} are independently selected amino acids, and

n is zero or one.

Claim 44 (Original): The composition of claim 43, wherein said polypeptide is not CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3).

Claim 45 (Original): A method of identifying a compound that modulates ligand binding to a melanocortin receptor, said method comprising: modeling test compounds that fit spatially into a melanocortin receptor ligand binding site of interest using an atomic structural model of a melanocortin receptor binding region or portion thereof; screening said test compounds in an assay characterized by binding of a test compound to a melanocortin receptor ligand binding site; and identifying a test compound that modulates ligand binding to said melanocortin receptor.

Claim 46 (Original): The method of claim 45, wherein said melanocortin receptor binding region comprises the minimized agouti related protein receptor binding region or portion thereof.

Claim 47 (Original): The method of claim 45, wherein said atomic structural model comprises atomic coordinates of amino acid residues corresponding to residues 1-18 of the N-terminal loop of the minimized agouti related protein (residues 1-18 of SEQ ID NO:2), residues 19-13 of the central loop of the minimized agouti related protein (residues 19-34 of SEQ ID NO:2), and residues 35-46 of the C-terminal loop of the minimized agouti related protein (residues 35-46 of SEQ ID NO:2).

Claim 48 (Original): The method of claim 45, wherein said atomic structural model comprises atomic coordinates of amino acid residues corresponding to residues 19-34 of the central loop of the minimized agouti related protein (residues 19-34 of SEQ ID NO:2) and at least residues 15-18 of the N-terminal loop of the minimized agouti related protein (residues 15-18 of SEQ ID NO:2).

Claim 49 (Original): The method of claim 45, wherein said atomic structural model comprises atomic coordinates of amino acid residues corresponding to residues 19-34 of the central loop of the minimized agouti related protein (residues 19-34 of SEQ ID NO:2) and at least 20% of the contiguous

or non-contiguous residues or their atoms are selected from residues 1-18 of the N-terminal loop of the minimized agouti related protein (residues 1-18 of SEQ ID NO:2).

Claim 50 (Original): The method of claim 45, wherein said atomic structural model comprises atomic coordinates of amino acid residues corresponding to residues 24-31 of the active loop of the minimized agouti related protein (residues 24-31 of SEQ ID NO:2).

Claim 51 (Original): The method of claim 45, wherein said atomic structural model comprises atomic coordinates of amino acid residues corresponding to residues 25-27 of the active loop of the minimized agouti related protein (residues 25-27 of SEQ ID NO:2).

Claim 52 (Original): The method of claim 45, wherein said screening is in vitro.

Claim 53 (Original): The method of claim 52, wherein said screening is high throughput screening.

Claim 54 (Original): The method of claim 45, wherein said assay is a biological assay.

Claim 55 (Original): The method of claim 45, wherein said test compound is from a library of compounds.

Claim 56 (Original): The method of claim 45, wherein said test compound is an agonist or antagonist of ligand binding.

Claim 57 (Original): The method of claim 56, wherein said test compound is a small organic molecule, a peptide, or peptidomimetic.

Claim 58 (Original): A method for identifying an agonist or antagonist of ligand binding to a melanocortin receptor, said method comprising the steps of: providing the atomic coordinates of a melanocortin receptor binding region or portion thereof to a computerized modeling system; modeling compounds which match or mimic the receptor binding region and thus fit spatially into the melanocortin receptor ligand binding site; and identifying in an assay for melanocortin receptor activity a compound that increases or decreases the activity of said melanocortin receptor by binding the ligand binding site of said melanocortin receptor, whereby an agonist or antagonist of ligand binding is identified.

Claim 59 (Original): The method of claim 58, wherein said melanocortin receptor binding region comprises the minimized agouti related protein receptor binding region or portion thereof.

Claim 60 (Original): A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule that binds a melanocortin receptor comprising structure coordinates of amino acid residues corresponding to residues 1-18 of the N-terminal loop of the minimized agouti related protein (residues 1-18 of SEQ ID NO:2), residues 19-13 of the central loop of the minimized agouti related protein (residues 19-34 of SEQ ID NO:2), and residues 35-46 of the C-terminal loop of the minimized agouti related protein (residues 35-46 of SEQ ID NO:2), or a homologue of said molecule.

Claim 61 (Original): The machine readable storage medium of claim 60, wherein said molecule is a melanocortin receptor agonist.

Claim 62 (Original): The machine readable storage medium of claim 60, wherein said molecule is a melanocortin receptor antagonist.

Claim 63 (Original): The machine-readable data storage medium according to claim 60 herein said molecule is defined by the set of structure coordinates depicted in Table 4 or Table 5, or a homologue of said molecule, said homologue having a root mean square deviation from the backbone atoms of said amino acids of not more than 2.54Å.

Claim 64 (Original): A machine-readable data storage medium comprising a data storage material encoded with a first set of machine readable data which, when combined with a second set of machine readable data, using a machine programmed with instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data,, wherein: said first set of data comprises a Fourier transform of at least a portion of the structural coordinates selected from the group consisting of coordinates depicted in Table 4 or Table 5; and said second set of data comprises an X-ray diffraction pattern of a molecule.

Claim 65 (Original): An NMR structure of the minimized agouti related protein, embodied in a computer readable media.

Claim 66 (Original): A polypeptide comprising the amino acid sequence:

CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3)

or a modified form thereof, wherein said polypeptide is not a full-length AGRP and said polypeptide is not a MARP.

Claim 67 (Original): The polypeptide of claim 66, wherein the polypeptide is chemically synthesized.

Claim 68 (Original): A method of treating a disease state in mammals that is alleviated by treatment with a polypeptide having an amino acid sequence:

CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3)

which method comprises administering to a mammal in need of such a treatment a therapeutically effective amount of said polypeptide, or a pharmaceutically acceptable salt thereof.

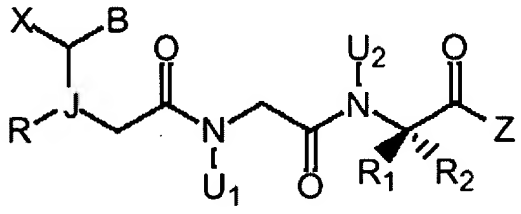
Claim 69 (Original): The method of claim 68, wherein said disease state is a wasting syndrome.

Claim 70 (Original): A pharmaceutical composition comprising a therapeutically effective amount of a polypeptide of the sequence:

CVRLHESCLGQQVPCCDPAATCYCRFFNAFCYC (SEQ ID NO:3)

or a pharmaceutically acceptable salt thereof.

Claim 71 (Original): A non-peptide melanocortin receptor ligand of the structural formula:



wherein

B, U_1, U_2, R, R_1, and R_2 are independently selected from the group consisting of: hydrogen, alkyl, derivatized alkyl, cycloalkyl, derivatized cycloalkyl, halocycloalkyl, aloxycycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl;

J is selected from the group consisting of carbon, nitrogen, silicon, and sulfur;

X is selected from the group consisting of hydrogen, carbon, nitrogen, oxygen, silicon, and sulfur; and

Z is selected from the group consisting of a continuing peptide bond, a hydroxyl; -NH2-, -NH-(n), and -N-(n,n'), and -O-(y), where where n and n' are independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, and a derivatized form thereof, and y is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl heteroarylalkyl, and a derivatized form thereof.

Claim 72 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand is a ligand for a melanocortin receptor selected from the group consisting of MC3r and MC4r.

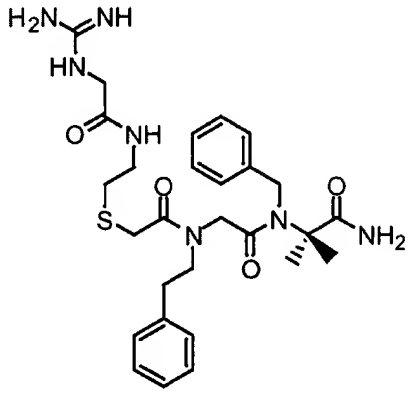
Claim 73 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand has a molecular weight ranging from about 200 to 1000 daltons.

Claim 74 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand has a structure that mimics the backbone of the AGRP active loop.

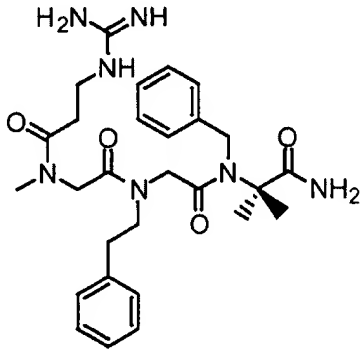
Claim 75 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand comprises a terminal gaunidino moiety.

Claim 76 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand comprises at least one methylbenzyl moiety.

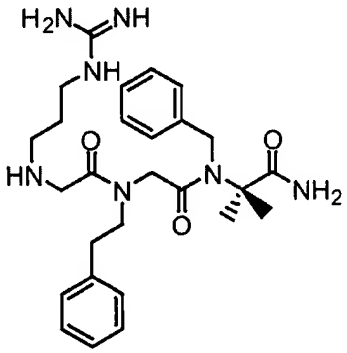
Claim 77 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand has the structural formula:



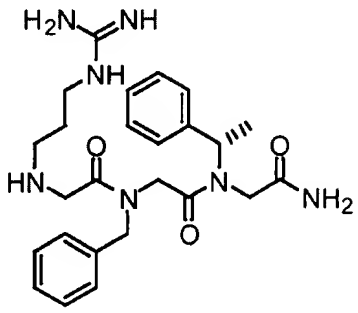
Claim 78 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand has the structural formula:



Claim 79 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand has the structural formula:



Claim 80 (Original): The non-peptide melanocortin receptor ligand according to claim 71, wherein said ligand has the structural formula:



Claim 81 (Original): A pharmaceutical preparation of a non-peptide melanocortin receptor ligand according to claim 71.

Claim 82 (Original): The pharmaceutical preparation according to claim 81, wherein said ligand is a melanocortin receptor antagonist.

Claim 83 (Original): The pharmaceutical preparation according to claim 82, wherein said ligand is a melanocortin receptor agonist.

Claim 84 (Original): A method for modulating a melanocortin receptor mediated physiological process, said method comprising:

contacting said melanocortin receptor with a non-peptide melanocortin receptor ligand according to claim 71.

Claim 85 (Original): The method according to claim 84, wherein said ligand is a melanocortin receptor agonist.

Claim 86 (Original): The method according to claim 84, wherein said ligand is a melanocortin receptor antagonist.